REMARKS

Amendments

Claims 1-27, 33-36, 38-46, 48-52 and 58 have been canceled, claims 28-32 and 55-57, and claims 59-63 have been added. Upon entry of the amendment, claims 28-32, 37, 47, 53-57 and 59-63 will be pending. Support for the amendments can be found in the specification, specifically on page 6, lines 28 through page 7, line 2; Example 1; the Figures, and in the claims as originally filed.

Rejections

Rejections under 35 U.S.C. §§ 101

The Examiner has rejected claims 28-32, 37, 47 and 52-58 and because the claimed invention is allegedly not supported by either a specific or substantial asserted utility or a well-established utility.

Applicant respectfully traverses the rejection. Amended claim 1 is drawn to a transgenic mouse whose genome comprises a null allele in the endogenous PTP36 gene.

1. Utility Requirement

Applicant incorporates and references arguments made in the amendment submitted February 17, 2005.

2. Well-Established Utility

According to 35 U.S.C. § 101, "[w]hoever invents . . . any new and useful . . . composition of matter may obtain a patent therefore. . . . "

Under the Patent Office's Utility Requirement Guidelines:

> If at any time during the examination, it becomes readily apparent that the claimed invention has a well-established utility, do not impose a rejection based on lack of utility. An invention has a well-established utility if (i) a person of ordinary skill in the art would immediately appreciate why the invention is useful based on the characteristics of the invention (e.g., properties or applications of a product or process), and (ii) the utility is specific, substantial, and credible.

Applicant submits that in light of arguments of record that a person of ordinary skill in the art would immediately appreciate why the invention is useful. Applicant submits that it

cannot be reasonably debated that a person of ordinary skill in the art would not immediately appreciate why the invention is useful: for determining gene function.

3. Specific

The Examiner argues that the asserted utility "applies to any knockout mouse is not specific to the claimed invention, the PTP36 knockout mouse" (page 8).

Applicant does not agree. "All knockout mice" cannot be used to study the function of the PTP36 gene. The use of each knockout mouse is specific to the particular gene which is disrupted.

According to the MPEP, "specific utility" means "specific" to the subject matter claimed as compared to a "general utility" that would be applicable to the broad class of the invention (MPEP 2107.01). Use of the PTP36 -/- mouse to study the function of the PTP36 gene and the association of the PTP36 gene with, for example, female sex organ development, is specific to this mouse. Even if there were many other genes associated with these conditions, only a PTP36 knockout mouse (as opposed to all other knockout mice) would be used to study the specific role of this gene in these conditions. The Examiner is respectfully requested to explain (1) how the asserted utility of characterizing the function of the PTP36 gene would be applicable to all other knockout mice; and (2) how the asserted use of studying the association of the PTP36 gene with female sex organ development would be applicable to all other knockout mice. The Examiner is requested to explain how all other knockout mice would be used to study the function of the PTP36 gene.

In addition, the mice within the scope of claim 57 contain a *lacZ* gene. Their use in studying gene expression is clearly recognized by those skilled in the art:

> **Null-reporter alleles should be created**
> The project should generate alleles that are as uniform as possible, to allow efficient production and comparison of mouse phenotypes. The alleles should achieve a balance of utility, flexibility, throughput and cost. A null allele is an indispensable starting point for studying the function of every gene. Inserting a reporter gene (e.g., P-galactosidase or green fluorescent protein) allows a rapid assessment of which cell types normally support the expression of that gene.

(Austin et al., Nature Genetics (2004) 36(9):921-24, 922)(emphasis in original; emphasis added)(copy attached). As cited in Austin, and as is well known by one of ordinary skill, the purpose of expression analysis is to determine where the gene is expressed.

As is well understood in the art, the *lacZ* gene is inserted into the endogenous gene. In this case, the *lacZ* gene was inserted into the locus of the PTP36 gene. Expression is driven by the endogenous promoter. Expression of the *lacZ* gene indicates where the PTP36 gene is expressed. This use is specific for this mouse – knockout mice in general cannot be used for this purpose. The Examiner is respectfully requested to explain how all other knockout mice would be used to study expression of the PTP36 gene.

4. Substantial

The Examiner argues that the asserted utilities are not substantial (page 8).

Applicant does not agree. According to the MPEP, under the section entitled "Substantial Utility":

> A "substantial utility" defines a "real world" use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities. . . . the following are examples of situations that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use and, therefore, do not define "substantial utilities":
>
> (A) Basic research such as studying the properties of the claimed product itself or the mechanisms in which the material is involved;
>
> Office personnel must be careful not to interpret the phrase "immediate benefit to the public" or similar formulations in other cases to mean that products or services based on the claimed invention must be "currently available" to the public in order to satisfy the utility requirement. See, e.g., Brenner v. Manson, 383 U.S. 519, 534-35, 148 USPQ 689, 695 (1966). Rather, **any reasonable use** that an applicant has identified for the invention that can be viewed as providing a public benefit **should be accepted as sufficient,** at least with regard **to defining a "substantial" utility.**

(MPEP § 2107.01 I)(emphasis added).

The MPEP additionally provides:

> Some confusion can result when one attempts to label certain types of inventions as not being capable of having a specific and substantial utility based on the setting in which the invention is to be used. One example is inventions to be used in a research or laboratory setting. Many research tools such as gas chromatographs, screening assays, and nucleotide sequencing techniques have a clear, specific and unquestionable utility

> (e.g., the are useful in analyzing compounds). An assessment that focuses on whether an invention is useful only in a research setting thus does not address whether the invention is in fact "useful" in a patent sense. Instead, Office personnel must distinguish between inventions that have a specifically identified substantial utility and inventions whose asserted utility requires further research to identify or reasonably confirm. Labels such as "research tool," "intermediate" or "for research purposes" are not helpful in determining if an applicant has identified a specific and substantial utility for the invention.
>
> (MPEP 2107.01, I)

A use is not substantial where further research is required to identify any use. This is not the case in the present application. Knockout mice have a well-known use in the study of gene function. In the present case, the instant invention does not require further research to establish a utility. Applicant has determined that the PTP36 gene is associated with, for example, female sex organ development. No further research is required to establish any use. Whether additional research is required to identify therapeutic agents targeting the PTP36 gene or to further characterize the function of the PTP36 gene is irrelevant to whether the claimed invention has satisfied the utility requirement.

Commercial use and acceptance is an important indication that the utility of an invention has been recognized by one of skill in the art ("A patent system must be related to the world of commerce rather than to the realm of philosophy." *Brenner v Manson*, 383 U.S. 519, 148 U.S.P.Q. 689, 696 (1966)). Commercial use of the knockout mice produced by Assignee Deltagen has been clearly established. The claimed mouse has been extensively analyzed using the tests set forth in the Examples. This data has been incorporated into Deltagen's commercial database product, DeltaBase. This database has been subscribed to by at least three of the world's largest pharmaceutical companies, Merck, Pfizer and GSK. In addition, at least one (1) pharmaceutical company has ordered the presently claimed mouse. This acceptance more than satisfies the practical utility requirement of section 101 as **it cannot be reasonably argued that a claimed invention which is actually being used by those skilled in the art has no "real world" use**. (see, for example, Phillips Petroleum Co. v. U.S. Steel Corp., 673 F. Supp. 1278, 6 U.S.P.Q.2d 1065, 1104 (D. Del. 1987), *aff'd*, 865 F.2d 1247, 9 U.S.P.Q.2d 1461 (Fed. Cir. 1980)("lack of practical utility cannot co-exist with infringement and commercial success);

(Lipscomb's Walker on Patents, §5:17, p. 562 (1984)("Utility may be evidenced by sales and commercial demand.")

Applicant is submitting herewith, as evidence of such sales and purpose of such use, a Rule 132 Declaration from Robert Driscoll, Vice President of Intellectual Property & Legal Affairs of Assignee, Deltagen.

The Examiner asserts the claimed mice are not useful as research tools because using a product for further research is not a "substantial utility;" and that further study would be required to determine the function of the gene (page 8).

Applicant does not agree. First, it is wholly untrue that further research is required in order to confirm the utility of the claimed mouse in determining the function of PTP36 gene. The value of knockout mice in determining gene function is well established and accepted in the art. This is demonstrated by the references cited above. The Examiner has failed to provide sufficient factual support for the position that it is more likely than not that a person of skill in the art would doubt that Applicant's asserted utility is specific and substantial, which is the standard for establishing a *prima facie* case. See MPEP § 2107.02, IV.

Second, Applicant is claiming a transgenic mouse, and not PTP36 or nucleic acid sequence. The Examiner must differentiate between the utility of the transgenic mouse and the utility of the target gene. "The claimed invention is the focus of the assessment of whether an applicant has satisfied the utility requirement." (MPEP 2107.02, I) That the claimed transgenic mouse can be used in a research setting to further characterize the PTP36 gene does not mean that the mouse lacks patentable utility. Further characterization (involving "basic research") of the mouse itself is not necessary in order to confirm its utility in studying the function of the PTP36 gene.

According to the MPEP:

> **any reasonable use** that an applicant has identified for the invention that can be viewed as providing a public benefit **should be accepted as sufficient,** at least with regard to defining a "substantial" utility.

Certainly providing an *in vivo* model for studying the function of the PTP36 gene is a reasonable use.

In addition, the MPEP specifically cautions Examiners not to get confused by labeling inventions as research tools:

> Office personnel must distinguish between inventions that have a specifically identified substantial utility and inventions whose asserted utility requires further research to identify or reasonably confirm. Labels such as "research tool," "intermediate" or "for research purposes" are not helpful in determining if an applicant has identified a specific and substantial utility for the invention.

Applicant respectfully submits that the Examiner has done what the MPEP specifically cautions against, by providing: "[a]n assessment that focuses on whether an invention is useful only in a research setting thus does not address whether the invention is in fact "useful" in a patent sense."

The Examiner argues that scientific "utility" is not the same as "patentable utility" or a "well-established" utility (page 8).

Applicant does not agree. According the Utility Guidelines,

> If the applicant has asserted that the claimed invention is useful for any particular practical purpose (i.e., it has a "specific and substantial utility") and the assertion would be considered credible by a person of ordinary skill in the art, do not impose a rejection based on lack of utility.

As acknowledged by the Examiner, the use of knockout mice to study gene function is well-known – i.e., the mouse has scientific utility. If the asserted use is considered credible and accepted by the scientific community, the use is by definition substantial. Applicant submits that if a claimed invention has scientific utility, it necessarily follows that the invention has patentable utility.

5. In re Brana

The Examiner also argues that the fact pattern in *Brana* does not apply to the fact pattern of the instant application because in *Brana* the specification did disclose a specific and substantial use for the claimed compound (p. 11).

Applicant submits that the legal principles as well as the facts of *Brana* are applicable to the present case. In *Brana*, the Board held that the applicant's specification failed to disclose a specific disease against which the claimed compounds were useful. The Federal Circuit reversed and held that the mouse tumor model represented a specific disease against which the compounds were effective. In the present case, the Examiner has argued that Applicant failed to

demonstrate a link between the PTP36 gene and any of the recited phenotypes. It is Applicant's position that a mouse demonstrating, for example, abnormalities of the female sex organs, is sufficient to establish the animal's use as a model for female sex organ development, diseases and conditions. As in *Brana*, confirmation of the phenotype in humans is unnecessary.

As in *Brana*, the PTO did not regard the asserted use to be credible:

> Applicants' specification, however, also states that the claimed compounds have "a better action and a better action spectrum as antitumor substances" than known compounds, specifically those analyzed in Paull. As previously noted, see supra note 4, Paull grouped various benzo [de]isoquinoline-1,3-diones, which had previously been tested in vivo for antitumor activity against two lymphocytic leukemia tumor models (P388 and L1210), into various structural classifications and analyzed the test results of the groups (i.e. what percent of the compounds in the particular group showed success against the tumor models). Since one of the tested compounds, NSC 308847, was found to be highly effective against these two lymphocytic leukemia tumor models, 14 applicants' favorable comparison implicitly asserts that their claimed compounds are highly effective (i.e. useful) against lymphocytic leukemia. An alleged use against this particular type of cancer is much more specific than the vaguely intimated uses rejected by the courts in Kirk and Kawai. See, e.g., Cross v. Iizuka, 753 F.2d at 1048, 224 USPQ at 745 (finding the disclosed practical utility for the claimed compounds -- the inhibition of thromboxane synthetase in human or bovine platelet microsomes -- sufficiently specific to satisfy the threshold requirement in Kirk and Kawai.)
>
> The Commissioner contends, however, that P388 and L1210 are not diseases since the only way an animal can get sick from P388 is by a direct injection of the cell line. The Commissioner therefore concludes that applicants' reference to Paull in their specification does not provide a specific disease against which the claimed compounds can be used. We disagree.

(*Brana* at 1440). As in the present case, the PTO was aware of the asserted use against the mouse tumor lines but did not find the use specific.

The court went on:

> The ultimate issue is whether the Board correctly applied the Section 112 Para.1 enablement mandate and its implicit requirement of practical utility, or perhaps more accurately the underlying requirement of Section 101, to the facts of this case. As we have explained, the issue breaks down into two subsidiary issues: (1) whether a person of ordinary skill in the art would conclude that the applicants had sufficiently described particular diseases addressed by the invention, and (2) whether the Patent Act supports a requirement that makes human testing a prerequisite to patentability under the circumstances of this case.
>
> The first subsidiary issue, whether the application adequately described particular diseases, calls for a judgment about what the various representations and discussions

> contained in the patent application's specification would say to a person of ordinary skill in the art. We have considered that question carefully, and, for the reasons we explained above in some detail, we conclude that the Board's judgment on this question was erroneous. Our conclusion rests on our understanding of what a person skilled in the art would gather from the various art cited, and from the statements in the application itself. We consider the Board's error to be sufficiently clear that it is reversible whether viewed as clear error or as resulting in an arbitrary and capricious decision.
>
> The second subsidiary issue, whether human testing is a prerequisite to patentability, is a pure question of law: what does the practical utility requirement mean in a case of this kind. Under either our traditional standard or under the APA standard no deference is owed the Agency on a question of law, and none was accorded.
>
> If the question concerning the standard of review, raised by the Commissioner, is to be addressed meaningfully, it must arise in a case in which the decision will turn on that question, and, recognizing this, the parties fully brief the issue. This is not that case. We conclude that it is not necessary to the disposition of this case to address the question raised by the Commissioner; accordingly, we decline the invitation to do so.

(*Brana* at 1443-44). The court's position is reflected in the MPEP: if an "assertion would be considered credible by a person of ordinary skill in the art, do not impose a rejection based on lack of utility" (MPEP § 2107, II (A)(3); II (B)(1)). If it is well known to those skilled in the art that knockout mice are useful for studying gene function, then those skilled in the art would certainly regard such use as credible, specific and substantial. Nothing more is required to satisfy the statutory requirement. Applicant submits that, as in *Brana*, one skilled in the art would find the asserted use credible, substantial and specific.

In *Brana*, the court found a mouse with an implanted murine tumor to represent a specific disease. Applicant submits that the claimed mouse having with a null PTP36 gene and demonstrating sex organ abnormalities, likewise represents a specific disease.

6. Summary

In summary, Applicant submits that the claimed transgenic mouse, regardless of any disclosed phenotypes, has inherent and well-established utility in the study of the function of the gene, and thus satisfies the utility requirement of section 101. Moreover, Applicant believes that the transgenic mice are useful for studying the function of the target protease gene with respect to the cited phenotypes as well as studying gene expression; and are therefore useful for a specific practical purpose that would be readily understood by and considered credible by one of ordinary skill in the art.

In light of the amendments and arguments set forth above, Applicant does not believe that the Examiner has properly established a *prima facie* showing that establishes that it is more likely than not that a person of ordinary skill in the art would not consider that any utility asserted by the Applicant would be specific and substantial. (*In re Brana*; MPEP § 2107).

Withdrawal of the rejections is respectfully requested.

Rejection under 35 U.S.C. § 112, first paragraph

The Examiner has rejected the claims because one skilled in the art would allegedly not know how to use the claimed invention as a result of the alleged lack of either a specific or substantial asserted utility or a well-established utility for the reasons set forth in the utility rejection. Applicants respectfully traverse the rejection. For the reasons set forth above, it is Applicant's position that the claimed invention satisfies the utility requirement. Therefore, one skilled in the art would know how to use the invention.

The Examiner argues that "[f]or reasons set forth in the previous office actions and above, the 112 1st rejection is maintained" (page 12). The Examiner appears to be implying that the rejections were not fully responded to.

Claims 1-9 and 14-23 were initially rejected under 112(1) on the ground that the specification failed to teach "how to make and use" the claimed invention (Office Action mailed June 2003).

In their response, Applicants cancelled claims 1-9 and 14-23, and added claims 28-47.

According to the Examiner, the rejections with regard to claims 1-9 and 14-23 were rendered moot by their cancellation (Office Action mailed December 23, 2003, p. 2). The rejections under 112(1) were not applied to the newly added claims.

Subsequently, claims 28-47 were rejected under 112(1) for allegedly failing to teach "how to use" the claimed mice (Office Action mailed April 27, 2004, pp. 2-4). These were essentially arguments more properly made under 101/112(1) for lack of utility. Applicant points out that these rejections were fully responded to in the Amendment filed September 27, 2004 (pp. 5-9).

The rejection with regard to claims 28-47 under 112(1) was maintained in the Office Action mailed December 16, 2004. No additional arguments were made by the Examiner.

Although the Examiner referenced the Office Action mailed June 3, 2003, those rejections were never made with regard to the presently pending claims.

Thus, the only rejections made under 112(1) with regard to the pending claims, are based on alleged failure to teach "how to use" the claimed invention. Applicant submits that these rejections have been fully responded to.

Applicant submits that the specification fully enables the claimed invention and respectfully requests withdrawal of the rejections.

Rejection under 35 U.S.C. § 112, first paragraph

Claims 28-32, 37, 47, 52-54 and 57 stand rejected for allegedly failing to comply with the written description requirement.

The claims have been amended. Withdrawal of the rejection is respectfully requested.

Rejection under 35 U.S.C. § 112, second paragraph

Claim 32 has been rejected as allegedly being indefinite.

Claim 32 has been amended as per the Examiner's suggestion.

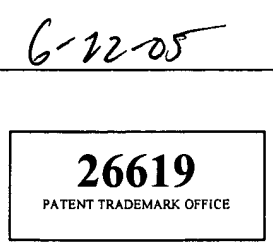
In view of the above amendments and remarks, Applicant respectfully requests a Notice of Allowance. If the Examiner believes a telephone conference would advance the prosecution of this application, the Examiner is invited to telephone the undersigned at the below-listed telephone number.

The Commissioner is hereby authorized to charge any deficiency or credit any overpayment to Deposit Account No. 502775.

Respectfully submitted,

6-12-05

Date



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